

WHAT IS CLAIMED IS:

1. A method of monitoring polymer array synthesis on a solid substrate comprising:

 - (i) providing a preselected array of labeled polymers connected to cleavable linkers on a solid substrate;
 - (ii) cleaving the array of labeled polymers from the solid substrate by cleaving the cleavable linkers, thereby creating labeled unbound polymers; and,
 - (iii) detecting the labeled unbound polymers.
2. The method of claim 1, wherein each of the labeled polymers comprise a single isomer.
3. The method of claim 1, wherein the labeled unbound polymers are heterogeneous by size, and wherein the method further comprises separating the labeled unbound polymers by size.
4. The method of claim 1, wherein the labeled unbound polymers are heterogeneous by size, and wherein the method further comprises separating the labeled unbound polymers by charge using ion exchange chromatography.
5. The method of claim 1, wherein the labeled unbound polymers are heterogeneous by size, and wherein the method further comprises separating the labeled unbound polymers by size using capillary gel electrophoresis.
6. The method of claim 4, wherein the ion exchange chromatography is performed by HPLC.

1 7. The method of claim 4, wherein the ion exchange
2 chromatography is performed by HPLC, and wherein the labeled unbound
3 polymers are detected as they exit an ion exchange column.

1 8. The method of claim 1, wherein the polymer is an
2 oligonucleotide.

1 9. The method of claim 1, wherein the preselected array of
2 polymers is provided by synthesizing polymers in an array.

1 10. A method for measuring the effect of altering a polymer array
synthesis protocol, comprising:

2 (i) providing an array of polymers synthesized on a solid support by
3 a first synthesis protocol, thereby creating a reference array of polymers;

4 (ii) providing an array of polymers on a solid support synthesized by
5 a second synthesis protocol, wherein the second synthesis protocol is different than
6 the first synthesis protocol, thereby creating a test array of polymers;

7 (iii) cleaving separately the reference array of polymers and the test
array of polymers, thereby creating cleaved reference polymers and cleaved test
10 polymers;

11 (iv) detecting the cleaved test polymers and the cleaved reference
polymers; and,

13 (v) comparing the cleaved test polymers to the cleaved reference
14 polymers.

1 11. The method of claim 10, wherein the test and reference
2 polymers are oligonucleotides.

1 12. The method of claim 10, wherein the first synthesis protocol
2 differs from the second synthesis protocol by a single variation.

1 13. The method of claim 10, wherein the reference polymers and
2 the test polymers are attached to the solid substrate by a cleavable linker.

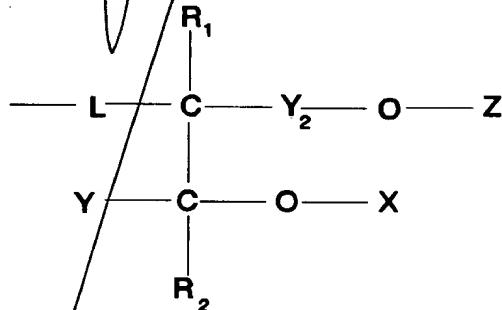
1 14. The method of claim 10, wherein the test and reference
2 polymers comprise a detectable label.

1 15. The method of claim 14, wherein the label is a single isomer.

1 16. A detectable monomeric polymer synthesis reagent with the
2 structure A-B, wherein A comprises a detectable chromogenic moiety and B
3 comprises a polymer integration element, said integration element comprising a
4 polymer joining agent selected from the group consisting of an amine; a carboxyl;
5 an oxygen; and a phosphate; and wherein A-B is a single isomer.

1 17. The polymer synthesis reagent of claim 16, wherein the
2 chromogenic moiety is a fluorophore.

1 18. The polymer synthesis reagent of claim 16, wherein the
2 polymer synthesis reagent is a nucleic acid synthesis reagent, wherein B comprises
3 the structure



5 and wherein

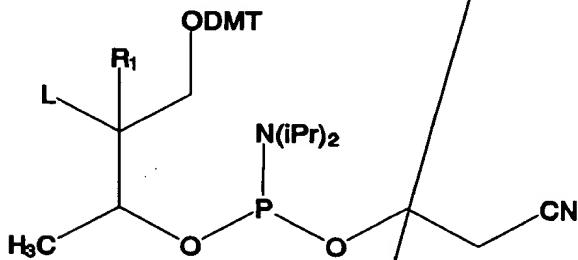
6 L is a linking chain selected from the group of linking chains
7 consisting of an alkyl linking chain from 1 to 30 carbons in length, wherein one or

8 more carbon is optionally substituted with a heteroatom selected from the group
 9 consisting of N, S, O and P, and wherein the alkyl linking group optionally
 10 includes one or more sites of unsaturation, and an alkyl linking chain from 1 to 30
 11 carbons in length, wherein one or more carbon is optionally replaced with a
 12 heteroatom selected from the group consisting of N, S, O and P, and wherein the
 13 alkyl linking group optionally includes one or more sites of unsaturation;

14 R₁ is selected from the group consisting of hydrogen, alkyl, and aryl;
 15 R₂ is selected from the group consisting of hydrogen, alkyl, and aryl;
 16 X is a nucleic acid integration element comprising a phosphorous
 17 atom,

18 Y is selected from the group consisting of hydrogen, alkyl, and aryl;
 19 Y₂ is an alkyl chain; and
 20 Z comprises a protecting group.

1 19. The polymer synthesis reagent of claim 16, wherein the
 2 polymer synthesis reagent is a nucleic acid synthesis reagent, wherein B comprises
 3 the structure



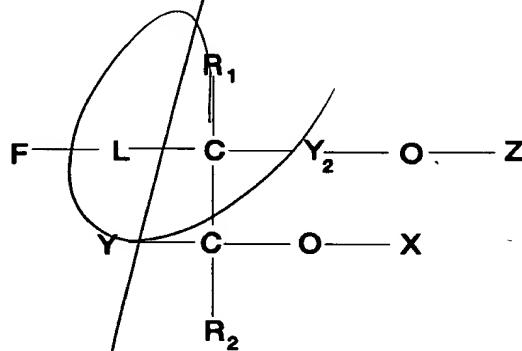
5 and wherein

6 L is selected from the group of alkyl linking chains consisting of an
 7 alkyl linking chain from 1 to 30 carbons in length, wherein one or more carbon is
 8 optionally substituted with a heteroatom selected from the group consisting of N,
 9 S, O and P, and wherein the alkyl linking group optionally includes one or more
 10 sites of unsaturation, and an alkyl linking chain from 1 to 30 carbons in length,
 11 wherein one or more carbon is optionally replaced with a heteroatom selected from

12 the group consisting of N, S, O and P, and wherein the alkyl linking group
 13 optionally includes one or more sites of unsaturation; and
 14 R₁ is selected from the group consisting of hydrogen, alkyl, and aryl.

1 20. A labeled oligonucleotide array attached to a solid substrate,
 2 wherein the oligonucleotides of the array comprise a single isomer of a detectable
 3 label.

1 21. A labeled oligonucleotide array attached to a solid substrate,
 2 wherein the label is a monoisomeric label comprising the structure



4 wherein
 5 F comprises a fluorescent group.

6 L is selected from the group of alkyl linking chains consisting of an
 7 alkyl linking chain from 1 to 30 carbons in length, wherein one or more carbon is
 8 optionally substituted with a heteroatom selected from the group consisting of N,
 9 S, O and P, and wherein the alkyl linking group optionally includes one or more
 10 sites of unsaturation, and an alkyl linking chain from 1 to 30 carbons in length,
 11 wherein one or more carbon is optionally replaced with a heteroatom selected from
 12 the group consisting of N, S, O and P, and wherein the alkyl linking group
 13 optionally includes one or more sites of unsaturation;

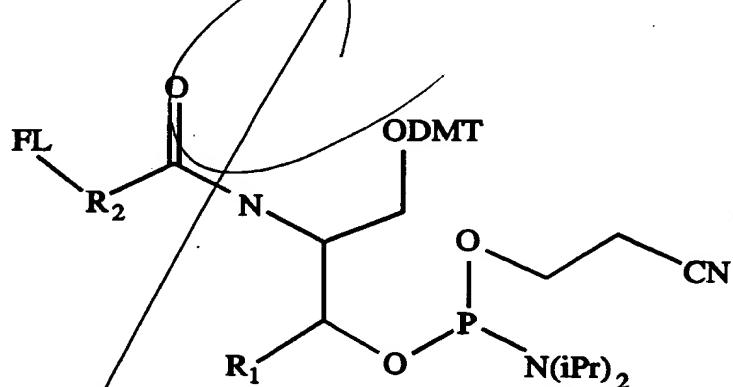
14 R₁ is selected from the group consisting of hydrogen, alkyl, and aryl;

15 R₂ is selected from the group consisting of hydrogen, alkyl, and aryl;

16 X is a nucleotide or a cleavable linker;

17 Y is selected from the group consisting of hydrogen, alkyl, and aryl;
18 Y₂ is selected from the group consisting of a hydrocarbon chain and a
19 substituted hydrocarbon chain; and,
20 Z is selected from the group consisting of a nucleotide and a nucleic
21 acid.

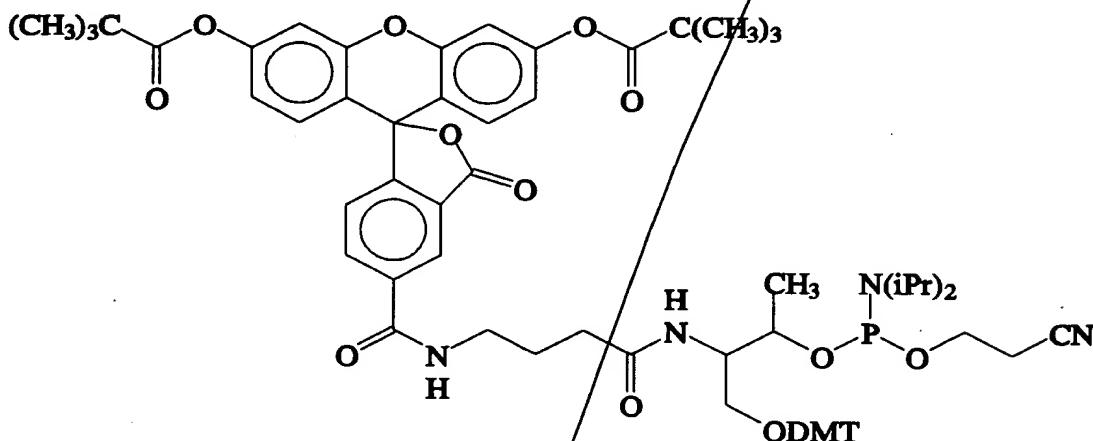
1 22. The nucleic acid synthesis reagent of claim 21, wherein the
2 nucleic acid synthesis reagent has the structure



4 wherein

5 R₁ is selected from the group consisting of alkyl, aryl, and hydrogen;
6 R₂ is selected from the group consisting of alkyl, and aryl; and
7 FL is a fluorescent moiety.

1 23. The isomeric nucleic acid synthesis reagent of claim 21,
 2 wherein the compound has the structure



1 24. The array of claim 21, wherein the composition further
 2 comprises a cleavable linker.

1 25. A method of post-synthetically labeling an oligonucleotide
 2 array, comprising:

- 3 (i) providing a polymer array which comprises a plurality of polymers,
 4 wherein each polymer comprises a labeling site; and
- 5 (ii) attaching a detectable label to the labeling site.

1 26. The method of claim 25, wherein the detectable label
 2 comprises a fluorophore.

1 27. The method of claim 25, wherein step (i) of said method
 2 comprises synthesizing a polymer array, which polymer array comprises polymers
 3 attached to a substrate, said polymers comprising a labeling linker, which labeling
 4 linker comprises an attachment site for the detectable label.

1 28. The method of claim 25, wherein step (i) of said method
 2 comprises synthesizing a polymer array, which polymer array comprises polymers

1 attached to a substrate, said polymers comprising a cleavable linker and a labeling
2 linker, which labeling linker comprises an attachment site for the detectable label,
3 a site for attachment to the cleavable linker and a protected site for the attachment
4 of the detectable label.

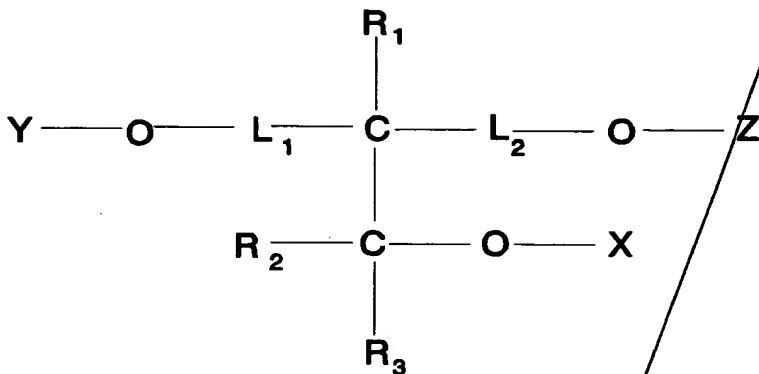
1 **29.** The method of claim 25, wherein step (i) of said method
2 comprises synthesizing a polymer array, which polymer array comprises polymers
3 attached to a substrate, said polymers comprising a cleavable linker and a labeling
4 linker, which labeling linker comprises a protected attachment site for the
5 detectable label, and wherein step (ii) of the method comprises deprotecting the
6 labeling linker, thereby making the protected attachment site into an unprotected
7 attachment site, and incubating the polymer array with a detectable labeling
8 reagent, which detectable labeling reagent comprises a site which is reactive with
9 the unprotected attachment site, and which labeling reagent comprises the
10 detectable label.

1 **30.** The method of claim 29, wherein said protected attachment
2 site comprises a DMT protective group.

1 **31.** The method of claim 25, wherein said labeling site is located
2 proximal to a cleavage site in the polymers of the polymer array.

1 **32.** A post-synthetic labeling linker which comprises a site for
2 polymer elongation, a site for attaching a polymer to a substrate and an attachment
3 site for attaching a detectable label.

1 33. The labeling linker of claim 32, wherein the linker has the
 2 structure



4 wherein:

5 R₁ is selected from the group consisting of hydrogen, alkyl and aryl;

6 R₂ is selected from the group consisting of hydrogen, alkyl and aryl;

7 R₃ is selected from the group consisting of hydrogen, alkyl and aryl,

8 L₁ is a linking chain selected from the group of alkyl linking chains

9 consisting of an alkyl linking chain from 1 to 30 carbons in length, wherein one or
 10 more carbon is optionally substituted with a heteroatom selected from the group
 consisting of N, S, O and P, and wherein the alkyl linking group optionally
 11 includes one or more sites of unsaturation, and an alkyl linking chain from 1 to 30
 12 carbons in length, wherein one or more carbon is optionally replaced with a
 13 heteroatom selected from the group consisting of N, S, O and P, and wherein the
 14 alkyl linking group optionally includes one or more sites of unsaturation;

15 L₂ is a linking chain selected from the group of alkyl linking chains

16 consisting of an alkyl linking chain from 1 to 30 carbons in length, wherein one or
 17 more carbon is optionally substituted with a heteroatom selected from the group
 consisting of N, S, O and P, and wherein the alkyl linking group optionally
 18 includes one or more sites of unsaturation, and an alkyl linking chain from 1 to 30
 19 carbons in length, wherein one or more carbon is optionally replaced with a
 20 heteroatom selected from the group consisting of N, S, O and P, and wherein the
 21 alkyl linking group optionally includes one or more sites of unsaturation;

1 Y is selected from the group consisting of a dimethoxytrityl protecting
2 group and a photocleavable protecting group;

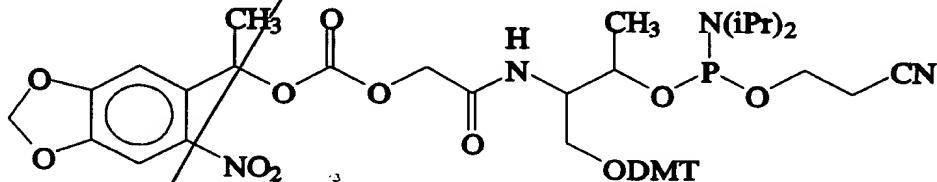
3 Z is selected from the group consisting of a dimethoxytrityl protecting
4 group and a photocleavable protecting group; and

5 X is a nucleic acid integration element comprising a phosphorous atom.

1 34. The labeling linker of claim 33, wherein Z is the
2 photocleavable group MeNPOC.

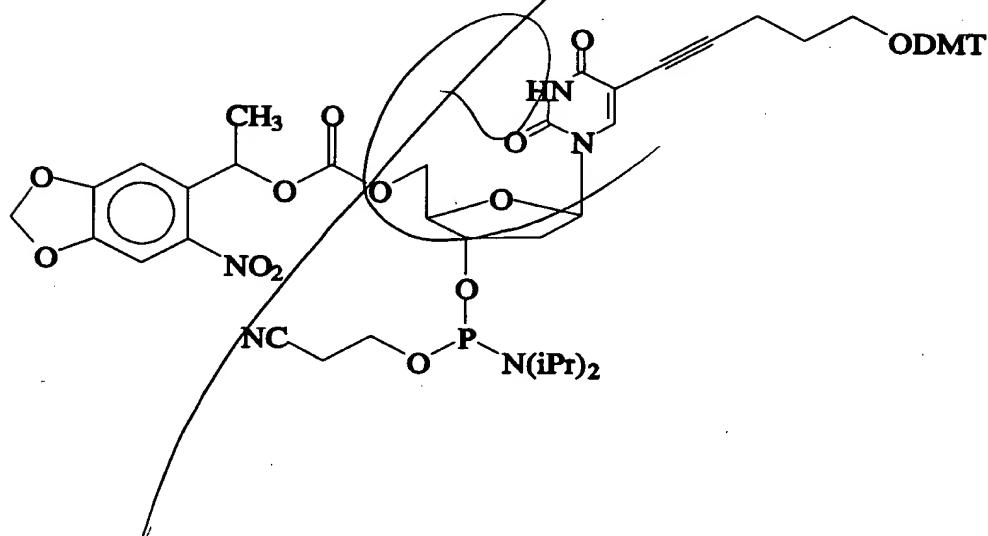
1 35. The labeling linker of claim 32, wherein the linker has the

2 structure



1 36. The labeling linker of claim 32, wherein the linker has the

2 structure



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